IMMUNE CELL COMPOSITIONS AND METHODS OF USE FOR TREATING VIRAL AND OTHER INFECTIONS

1. CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional application No. 62/381,219, filed Aug. 30, 2016, and U.S. Provisional application No. 62/468,881, filed Mar. 8, 2017, each of which is incorporated by reference herein in its entirety.

2. REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0002] This application incorporates by reference a Sequence Listing with this application as an ASCII text file entitled "13542-038-228_SL.TXT" created on Aug. 22, 2017, and having a size of 59,378 bytes.

3. FIELD

[0003] The present invention relates generally to treating viral infections, and more specifically to immunotherapy for treating viral infections.

4. BACKGROUND

[0004] Viral infections are known to cause a wide range of diseases. An acute viral infection is characterized by viral replication, spread, secondary replication, tissue damage and shedding (Virgin et al., *Cell* 138(1):30-50 (2009)). If the infected subject survives the acute viral infection, either the host immune system clears the infection, or the infection becomes persistent.

[0005] Persistent viral infections are characterized as viral infections that are not cleared from an individual but remain or persist in cells of the individual (see Boldogh et al., "Persistent Viral Infections" in *Medical Microbiology,* 4th ed., Baron, editor, Chapter 46, The University of Texas Medical Branch at Galveston (1996); Virgin et al., *Cell* 138(1):30-50 (2009)). Persistent viral infections can be classified as latent, chronic or slow infections (Boldogh et al., supra, 1996).

[0006] Latent infections lack demonstrable infectious virus between episodes of recurrent disease. In chronic infection, continued presence of infectious virus follows the primary infection and may include chronic or recurrent disease. Slow infection involves a prolonged incubation period followed by progressive disease (Boldogh et al., supra, 1996). Unlike latent and chronic infections, slow infection does not necessarily begin with an acute period of viral multiplication. During persistent infections, the viral genome can be stably integrated into the cellular DNA or maintained episomally (see Boldogh et al., supra, 1996).

[0007] A number of viral infections have a tendency to become persistent infections. Examples of such viral infections include infection with human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV). Infection with human immunodeficiency virus (HIV) can lead to acquired immunodeficiency syndrome (AIDS) and related medical conditions (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 1837-1891, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1791-1856, McGraw-Hill, San Francisco Calif. (1998)). Infection with hepatitis B virus (HBV), which predominantly affects the liver, can lead to progressive chronic liver disease with cirrhosis and, in some cases, hepatocellular carcinoma (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 762-767, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1677-1681, McGraw-Hill, San Francisco Calif. (1998)). Infection with hepatitis C virus (HCV), which also predominantly affects the liver, also can lead to progressive chronic liver disease with cirrhosis and, in some cases, hepatocellular carcinoma (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 762-764, 767-769, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1677, 1681-1682, McGraw-Hill, San Francisco Calif. (1998)). Such viral infections can lead to persistent infections.

[0008] Other viral infections include infection with herpes simplex virus (HSV), varicella zoster virus or (VZV), adenovirus, cytomegalovirus (CMV), and Epstein-Barr Virus (EBV). Infection with HSV can lead to gingivostomatitis, usually caused by HSV-1, for example, herpes simplex labialis (cold sores) (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 1770-1774, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1080-1086, McGraw-Hill, San Francisco Calif. (1998)). Infection with HSV can also cause genital herpes, most commonly caused by HSV-2; herpetic keratitis, usually caused by HSV-1 and often accompanied by conjunctivitis; neonatal HSV infection, usually caused by HSV-2; and herpes simplex encephalitis, usually caused by HSV-1. Infection with HSV can become a latent infection (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 1770-1774, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1080-1086, McGraw-Hill, San Francisco Calif. (1998)).

[0009] Infection with VZV can cause chickenpox (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 1763-1765, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1086-1089, McGraw-Hill, San Francisco Calif. (1998)). Latent infections can evolve to herpes zoster (shingles) caused by reactivation of VZV that is normally latent in sensory ganglia (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 2093-2095, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1086-1089, McGraw-Hill, San Francisco Calif. (1998)). Infection with adenovirus can cause disease in a variety of human epithelial tissues including the eye (pharyngoconjunctival fever; epidemic keratoconjunctivitis), respiratory tract, including upper respiratory tract illness (acute pharyngitis; exudative tonsillitis) and lower respiratory tract (pneumonia), urinary disease (hemorrhagic cystitis), and gastrointestinal disease (gastroenteritis) (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 1757-1759, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1104-1105, McGraw-Hill, San Francisco Calif. (1998)).

[0010] Infection with CMV can cause infectious mononucleosis and congenital infection (Bennett et al., *Cecil Textbook of Medicine,* 20th ed., pp. 1774-1776, W.B. Saunders, Philadelphia Pa. (1996); Fauci et al., *Harrison's Principles of Internal Medicine,* 14th ed., pp. 1092-1095, McGraw-Hill, San Francisco Calif. (1998)). Infection with EBV can cause infectious mononucleosis, including chronic mononucleosis or chronic fatigue syndrome, and latent EBV